WEST Search History

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DATE: Thursday, January 31, 2008

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT; PLUR=YES; OP=OR	
☐	L1	(antibod? and (sepsis or septic adj shock adj syndrome or septic adj shock) and tissue adj factor and factor adj x and (factor adj VII or factor adj VIIa) and monoclonal and chimeric and human and single adj chain and humanized)	121

END OF SEARCH HISTORY

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NEWS 2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS 6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 7	AUG 27	USPATOLD now available on STN
NEWS 8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 10	SEP 13	FORIS renamed to SOFIS
NEWS 11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS 12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS 13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS 14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS 16	OCT 19	BEILSTEIN updated with new compounds
NEWS 17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 18	NOV 19	WPIX enhanced with XML display format
NEWS 19	NOV 30	ICSD reloaded with enhancements
NEWS 20	DEC 04	LINPADOCDB now available on STN
NEWS 21	DEC 14	BEILSTEIN pricing structure to change
NEWS 22	DEC 17	USPATOLD added to additional database clusters
NEWS 23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 24	DEC 17	DGENE now includes more than 10 million sequences
NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 29	JAN 02	STN pricing information for 2008 now available
NEWS 30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 32	JAN 28	MARPAT searching enhanced
NEWS 33	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 34	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 35	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements

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 NEWS EXPRESS  19 SEPTEMBER 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE 'HOME' ENTERED AT 14:53:11 ON 31 JAN 2008

=> file medline embase biosis caplus
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                               ENTRY    SESSION
FULL ESTIMATED COST                             0.21       0.21

FILE 'MEDLINE' ENTERED AT 14:53:22 ON 31 JAN 2008

FILE 'EMBASE' ENTERED AT 14:53:22 ON 31 JAN 2008
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FILE 'BIOSIS' ENTERED AT 14:53:22 ON 31 JAN 2008
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FILE 'CAPLUS' ENTERED AT 14:53:22 ON 31 JAN 2008
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=> s (antibod? and (sepsis or septic(w)shock(w)syndrome or septic(w)shock) and
tissue(w)factor and factor(w)x and (factor(w)VII or factor(w)VIIa) and monoclonal
and chimeric and human and single(w)chain and humanized)
L1             0 (ANTIBOD? AND (SEPSIS OR SEPTIC(W) SHOCK(W) SYNDROME OR SEPTIC(W
                 ) SHOCK) AND TISSUE(W) FACTOR AND FACTOR(W) X AND (FACTOR(W)
                 VII OR FACTOR(W) VIIA) AND MONOCLONAL AND CHIMERIC AND HUMAN
                 AND SINGLE(W) CHAIN AND HUMANIZED)

=> s (antibod? and (sepsis or septic(w)shock(w)syndrome or septic(w)shock) and
tissue(w)factor and factor(w)x and (factor(w)VII or factor(w)VIIa)
UNMATCHED LEFT PARENTHESIS '(ANTIBOD?'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s antibod? and (sepsis or septic(w)shock(w)syndrome or septic(w)shock) and
tissue(w)factor and factor(w)x and (factor(w)VII or factor(w)VIIa)
L2            18 ANTIBOD? AND (SEPSIS OR SEPTIC(W) SHOCK(W) SYNDROME OR SEPTIC(W)
                  SHOCK) AND TISSUE(W) FACTOR AND FACTOR(W) X AND (FACTOR(W) VII
                 OR FACTOR(W) VIIA)

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3            11 DUP REM L2 (7 DUPLICATES REMOVED)

=> dis ibib abs l3 1-11
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L3 ANSWER 1 OF 11 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005661395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16100288
TITLE: Blockade of tissue factor-factor X binding attenuates sepsis-induced respiratory and renal failure.
AUTHOR: Welty-Wolf Karen E; Carraway Martha S; Ortel Thomas L; Ghio Andrew J; Idell Steven; Egan Jack; Zhu Xiaoyun; Jiao Jin-an; Wong Hing C; Piantadosi Claude A
CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, Duke University Medical Center, Durham, North Carolina 27710, USA.. welty001@mc.duke.edu
CONTRACT NUMBER: P01-HL-31992-18 (United States NHLBI)
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2006 Jan) Vol. 290, No. 1, pp. L21-31. Electronic Publication: 2005-08-12. Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 18 Dec 2005 Last Updated on STN: 21 Jan 2006 Entered Medline: 20 Jan 2006

AB Tissue factor expression in sepsis activates coagulation in the lung, which potentiates inflammation and leads to fibrin deposition. We hypothesized that blockade of factor X binding to the tissue factor-factor VIIa complex would prevent sepsis-induced damage to the lungs and other organs. Acute lung injury was produced in 15 adult baboons primed with killed Escherichia coli [1 x 10(9) colony-forming units (CFU)/kg], and then 12 h later, they were given 1 x 10(10) CFU/kg live E. coli by infusion. Two hours after live E. coli, animals received antibiotics with or without monoclonal antibody to tissue factor intravenously to block tissue factor-factor X binding. The animals were monitored physiologically for 34 h before being killed and their tissue harvested. The antibody treatment attenuated abnormalities in gas exchange and lung compliance, preserved renal function, and prevented tissue neutrophil influx and bowel edema relative to antibiotics alone (all $P < 0.05$). It also attenuated fibrinogen depletion ($P < 0.01$) and decreased proinflammatory cytokines, e.g., IL-6 and -8 ($P < 0.01$), in systemic and alveolar compartments. Similar protective effects of the antibody on IL-6 and -8 expression and permeability were found in lipopolysaccharide-stimulated endothelial cells. Blockade of factor X binding to the tissue factor -factor VIIa complex attenuates lung and organ injuries in established E. coli sepsis by attenuating the neutrophilic response and inflammatory pathways.

L3 ANSWER 2 OF 11 EMBASE
ACCESSION NUMBER: 2006225825 EMBASE
TITLE: Blockade of tissue factor-factor X binding attenuates sepsis-induced respiratory and renal failure.
AUTHOR: Welty-Wolf K.E.; Carraway M.S.; Ortel T.L.; Ghio A.J.; Idell S.; Egan J.; Zhu X.; Jiao J.-A.; Wong H.C.; Piantadosi C.A.
CORPORATE SOURCE: K.E. Welty-Wolf, Dept. of Medicine, Box 3518, Duke Univ.

Medical Center, Durham, NC 27710, United States.
welty001@mc.duke.edu

SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (Jan 2006) Vol. 290, No. 1, pp. L21-L31.
Refs: 39
ISSN: 1040-0605 E-ISSN: 1522-1504 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
028 Urology and Nephrology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jun 2006
Last Updated on STN: 1 Jun 2006

AB Tissue factor expression in sepsis activates coagulation in the lung, which potentiates inflammation and leads to fibrin deposition. We hypothesized that blockade of factor X binding to the tissue factor-factor VIIa complex would prevent sepsis-induced damage to the lungs and other organs. Acute lung injury was produced in 15 adult baboons primed with killed Escherichia coli [1 x 10(9) colony-forming units (CFU)/kg], and then 12 h later, they were given 1 x 10(10) CFU/kg live E. coli by infusion. Two hours after live E. coli, animals received antibiotics with or without monoclonal antibody to tissue factor intravenously to block tissue factor-factor X binding. The animals were monitored physiologically for 34 h before being killed and their tissue harvested. The antibody treatment attenuated abnormalities in gas exchange and lung compliance, preserved renal function, and prevented tissue neutrophil influx and bowel edema relative to antibiotics alone (all $P < 0.05$). It also attenuated fibrinogen depletion ($P < 0.01$) and decreased proinflammatory cytokines, e.g., IL-6 and -8 ($P < 0.01$), in systemic and alveolar compartments. Similar protective effects of the antibody on IL-6 and -8 expression and permeability were found in lipopolysaccharide-stimulated endothelial cells. Blockade of factor X binding to the tissue factor -factor VIIa complex attenuates lung and organ injuries in established E. coli sepsis by attenuating the neutrophilic response and inflammatory pathways. Copyright .COPYRGT. 2006 the American Physiological Society.

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:412830 CAPLUS
DOCUMENT NUMBER: 141:12270
TITLE: Pharmaceutical composition comprising a tissue factor antagonist and a blood glucose regulator for treating thrombosis and other diseases
INVENTOR(S): Petersen, Lars Christian; Back, Jakob Michael; Meyer, Christian
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004041302 A1 20040521 WO 2003-DK751 20031104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003275947 A1 20040607 AU 2003-275947 20031104
US 2004143099 A1 20040722 US 2003-701294 20031104
PRIORITY APPLN. INFO.: DK 2002-1710 A 20021106
US 2002-434904P P 20021220
WO 2003-DK751 W 20031104

AB The present invention relates to a composition comprising a TF antagonist and a blood glucose regulator, and the use thereof for treating Thrombotic or Coagulopathic related diseases, Respiratory diseases and Inflammatory diseases.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:995712 CAPLUS
DOCUMENT NUMBER: 141:423317
TITLE: Anti-human tissue factor antibodies for inhibiting blood coagulation and preventing and treating septic shock, inflammation and thrombosis
INVENTOR(S): Wong, Hing C.; Jiao, Jin-An
PATENT ASSIGNEE(S): Sunol Molecular Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 293,417.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229282	A1	20041118	US 2004-764140	20040122
US 5986065	A	19991116	US 1997-814806	19970310
US 2002168357	A1	20021114	US 1999-293854	19990416
US 6555319	B2	20030429		
US 2003082636	A1	20030501	US 2002-293417	20021112
WO 2005072126	A2	20050811	WO 2005-US1116	20050112
WO 2005072126	A3	20070518		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, AP, EA, EP, OA

US 2005271664 A1 20051208 US 2005-87528 20050322
PRIORITY APPLN. INFO.: US 1997-814806 A1 19970310
US 1999-293854 A1 19990416
US 2002-293417 A2 20021112

US 2004-764140 A 20040122

AB Disclosed is a method for treating blood coagulation in a mammal that has or is suspected of having septic shock syndrome. In one embodiment, the method includes administering to the mammal an effective amount of an antibody that binds tissue factor in a way that excludes Factor X (FX) binding. The invention has a wide range of useful applications including use to inhibit unwanted blood coagulation associated with sepsis, or blood clot or thrombosis associated with invasive medical procedure such as surgery or transplant or medical implementation (catheter, stent or other medical device). The antibodies may also be combined with anticoagulant, anti-platelet and/or thrombolytic agent to boost or prolong inhibition of blood coagulation.

L3 ANSWER 5 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004444628 EMBASE
TITLE: Tissue factor: (Patho)physiology and cellular biology.
AUTHOR: Eilertsen K.-E.; Osterud B.
CORPORATE SOURCE: Dr. K.-E. Eilertsen, Department of Biochemistry, Institute of Medical Biology, University of Tromso, N-9037 Tromso, Norway. Karl-Erik.Eilertsen@fagmed.uit.no
SOURCE: Blood Coagulation and Fibrinolysis, (Oct 2004) Vol. 15, No. 7, pp. 521-538.
Refs: 236
ISSN: 0957-5235 CODEN: BLFIE7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Nov 2004
Last Updated on STN: 4 Nov 2004

AB The transmembrane glycoprotein tissue factor (TF) is the initiator of the coagulation cascade in vivo. When TF is exposed to blood, it forms a high-affinity complex with the coagulation factors factor VII/activated factor VIIa (FVII/VIIa), activating factor IX and factor X, and ultimately leading to the formation of an insoluble fibrin clot. TF plays an essential role in hemostasis by restraining hemorrhage after vessel wall injury. An overview of biological and physiological aspects of TF, covering aspects consequential for thrombosis and hemostasis such as TF cell biology and biochemistry, blood-borne (circulating) TF, TF associated with microparticles, TF encryption - decryption, and regulation of TF activity and expression is presented. However, the emerging role of TF in the pathogenesis of diseases such as sepsis, atherosclerosis, certain cancers and diseases characterized by pathological fibrin deposition such as disseminated intravascular coagulation and thrombosis, has directed attention to the development of novel inhibitors of tissue factor for use as antithrombotic drugs. The main advantage of inhibitors of the TF.ovrhdot.FVIIa pathway is that such inhibitors have the potential of inhibiting the coagulation cascade at its earliest stage. Thus, such therapeutics exert minimal disturbance of systemic hemostasis since they act locally at the site of vascular injury. .COPYRGT. 2004 Lippincott Williams & Wilkins.

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:892884 CAPLUS
DOCUMENT NUMBER: 139:380016
TITLE: Novel tissue factor targeted antibodies as anticoagulants

INVENTOR(S): Light, David; McLean, Kirk
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003093422	A2	20031113	WO 2003-US13521	20030430
WO 2003093422	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2483910	A1	20031113	CA 2003-2483910	20030430
AU 2003225255	A1	20031117	AU 2003-225255	20030430
US 2004063632	A1	20040401	US 2003-427805	20030430
US 7250168	B2	20070731		
BR 2003004660	A	20050607	BR 2003-4660	20030430
EP 1549341	A2	20050706	EP 2003-721974	20030430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665526	A	20050907	CN 2003-815702	20030430
CN 1665534	A	20050907	CN 2003-815703	20030430
JP 2005532045	T	20051027	JP 2004-501558	20030430
NZ 536243	A	20060630	NZ 2003-536243	20030430
NO 2003005848	A	20040227	NO 2003-5848	20031230
IN 2004DN03332	A	20070112	IN 2004-DN3332	20041027
MX 2004PA10795	A	20050307	MX 2004-PA10795	20041029
ZA 2004009694	A	20060222	ZA 2004-9694	20041130
ZA 2004009692	A	20060726	ZA 2004-9692	20041130
US 2006166284	A1	20060727	US 2005-512215	20050112
US 2008019985	A1	20080124	US 2007-766155	20070621
US 2008020965	A1	20080124	US 2007-766160	20070621
PRIORITY APPLN. INFO.:			US 2002-376566P	P 20020501
			US 2003-427805	A1 20030430
			WO 2003-US13521	W 20030430

AB This invention relates to novel antibodies that bind with greater affinity to the factor VIIa/tissue factor (FVIIa/TF) complex than to tissue factor (TF) alone, do not compete for binding to TF with FVII and FX, and inhibit FX activation. The antibodies bind at the site of injury and prevent the initiation of thrombosis. The antibodies can be used to treat a variety of thrombotic conditions including but not limited to deep vein thrombosis, disseminated intravascular coagulation, and acute coronary syndrome.

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:315102 CAPLUS
DOCUMENT NUMBER: 136:337039
TITLE: Tissue factor pathway inhibitor Ixolaris from Ixodes scapularis
INVENTOR(S): Francischetti, Ivo M. B.; Valenzuela, Jesus G.; Ribeiro, Jose M.
PATENT ASSIGNEE(S): The Government of the United States of America, as

Represented by the Secretary, Department of Health and Human Services, USA

SOURCE: PCT Int. Appl., 213 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002033089	A2	20020425	WO 2001-US42472	20011005
WO 2002033089	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002030390	A5	20020429	AU 2002-30390	20011005
US 2004018516	A1	20040129	US 2003-408166	20030404
US 7078508	B2	20060718		

PRIORITY APPLN. INFO.: US 2000-240575P P 20001005
WO 2001-US42472 W 20011005

AB Ixolaris, a novel protein with anticoagulant activity is described. Ixolaris can be isolated from the salivary glands of ticks or made by recombinant methods using various DNA expression techniques. Following sequencing of an I. scapularis salivary gland cDNA library, a clone with sequence homol. to tissue factor pathway inhibitor (TFPI) was identified. This cDNA codes for a mature protein, called Ixolaris, with 140 amino acids containing 10 cysteines and two Kunitz-like domains. Recombinant Ixolaris inhibits Factor VIIa (FVIIA)-induced Factor X activation with an IC50 in the pM range. Ixolaris behaves as a fast-and tight ligand of FXa and des-Gla-FXa (γ-carboxyglutamic acid domainless FXa), increasing their esterolytic activity .apprx.2-fold. Ixolaris block the amidolytic activity of FVIIa/TF only in the presence of DEGR-FX or DEGR-FXa, but not des-Gla-DEGR-FXa. This result indicates that both FXa and FX are scaffolds for Ixolaris and implies that Gla-domain is necessary for Ixolaris/FX(a)/FVIIa/TF complex formation. Addnl., Ixolaris inhibits FIX activation by FVIIa/TF (Factor VIIa exosite inhibitor), and remarkable inhibition was achieved in the presence of FX/FXa. Western blotting using antibodies to Factor X and Factor VIIa shows that Ixolaris shifts the migration pattern of both Factor X and Factor Xa, but not Factor VIIa. Ixolaris is envisioned as being useful as an alternative anticoagulant in cardiovascular diseases as well as a vaccine target to prevent Lyme disease.

L3 ANSWER 8 OF 11 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002464222 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12223078
TITLE: Tissue factor - a therapeutic target for thrombotic disorders.
AUTHOR: Houston Donald S
CORPORATE SOURCE: Section of Hematology/Oncology, Department of Internal Medicine, University of Manitoba, 675 McDermot Avenue, Winnipeg, Manitoba, R3E 0V9, Canada..
houston@cc.umanitoba.ca
SOURCE: Expert opinion on therapeutic targets, (2002 Apr) Vol. 6,

No. 2, pp. 159-74. Ref: 154
Journal code: 101127833. E-ISSN: 1744-7631.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 12 Sep 2002
Last Updated on STN: 13 Dec 2002
Entered Medline: 12 Sep 2005

AB Exposure of blood to tissue factor (TF) sets off the coagulation cascade. TF is a transmembrane protein that serves as an essential cofactor for activated coagulation factor VII (FVIIa). TF may be exposed locally by vascular injury (such as balloon angioplasty) or by spontaneous rupture of an atherosclerotic plaque. Expression of TF may also be induced on monocytes and endothelial cells in conditions like sepsis and cancer, causing a more generalised activation of clotting. TF may thus play a central role in thrombosis in a number of settings, and attention has turned to blocking TF as a means to prevent thrombosis. Inhibiting the inducible expression of TF by monocytes can be achieved by 'deactivating' cytokines, such as interleukin (IL)-4, -10 and -13, or by certain prostanoids; by drugs that modify signal transduction, such as pentoxifylline, retinoic acid or vitamin D(3), or by antisense oligonucleotides. Such approaches are for the most part at a preclinical stage. The function of TF can be blocked by antibodies that prevent the binding of FVIIa to TF; by active site-inhibited FVIIa, which competes with native FVIIa for binding; by antibodies or small molecules that block the function of the TF/FVIIa complex; and by molecules, such as TF pathway inhibitor or nematode anticoagulant peptide C2, which inhibit the active site of FVIIa in the TF/FVIIa complex after first binding to activated factor X. The latter two agents have entered Phase II clinical trials. Perhaps most intriguing is the use of anti-TF agents locally, which holds the promise of stopping thrombosis at a specific site of injury without the bleeding risk associated with systemic anticoagulation.

L3 ANSWER 9 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:337305 BIOSIS
DOCUMENT NUMBER: PREV200300337305
TITLE: Induction of Microparticle and Cell-Associated Intravascular Tissue Factor in Human Endotoxemia.
AUTHOR(S): Aras, Omer [Reprint Author]; Shet, Arun [Reprint Author]; Hysjulien, Jessica L. [Reprint Author]; Escolar, Gines [Reprint Author]; Slungaard, Arne [Reprint Author]; Hebbel, Robert P. [Reprint Author]; Bach, Ronald R. [Reprint Author]; Jilma, Bernd [Reprint Author]; Key, Nigel S. [Reprint Author]
CORPORATE SOURCE: Medicine, University of Minnesota, Minneapolis, MN, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 198. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
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AB Tissue factor (TF) is the principal in vivo initiator of blood coagulation. Lipopolysaccharide (LPS) is a major trigger of disseminated intravascular coagulation in sepsis via the TF/

factor VIIa-dependent pathway of coagulation. In monocytes activated by LPS in vitro, increased TF synthesis is accompanied by release of microparticles (MPs) derived from the cell membrane. These MPs are highly procoagulant by virtue of their TF content and externally exposed anionic phospholipids. To assess the in vivo significance of these findings, we developed an assay for MP-associated TF procoagulant activity (PCA) in platelet poor plasma (PPP). The antibody 1B10 (which recognizes an undetermined antigen on human fibroblasts, monocytes, smooth muscle and endothelial cells) was used to capture MPs from PPP. MP-associated TF PCA was expressed as the concentration of factor Xa generated after the addition of factors VIIa and X to the captured, immobilized MPs. Most normal subjects had some detectable TF PCA that could be blocked by specific anti-TF antibodies. To test the hypothesis that LPS exposure in vivo leads to elevated whole blood and MP-associated TF PCA, we used a well defined human endotoxemia model. Whole blood TF PCA was measured using a previously described assay (Blood 91;4216,1998). Eighteen healthy male volunteers received 2ng/kg of LPS i.v.. Blood samples were obtained before and at various time points after endotoxin administration. Mean MP-associated TF PCA at baseline was 3.5+-3.4 pM/hr (mean+-SD). MP-associated TF PCA peaked at 3-4 hr (both $P<0.0001$ vs. baseline) after endotoxin administration, with return to baseline by 8 hr. Mean MP-associated TF PCA increased 8.2-fold over baseline, with considerable inter-individual variability, probably reflecting the well recognized in vitro phenomenon of 'high' and 'low' LPS responders. Mean whole blood TF PCA also increased in a time-dependent manner despite the transient peripheral blood monocytopenia. Peak whole blood TF PCA was observed at 4 hr, but in this case, the activity persisted up to 24 hr. A linear correlation between whole blood TF PCA and MP-associated TF PCA was observed ($r=0.342$, $P=0.0001$). Activation of coagulation was evident as a 7.6-fold increase in plasma levels of prothrombin fragment F1+2 at 4 hr ($P<0.00001$); values remained elevated at 8 hr ($P<0.01$), but returned to baseline by 24 hr. Plasma D-dimer levels increased about 4-fold at 4, 8, and 24 hr after LPS infusion ($P=0.004$, $P=0.001$, $P<0.0001$ respectively). By flow cytometry, increased numbers of circulating MPs were present at 4 hr, and it was demonstrated that these MPs were primarily derived from CD14+ monocytes, with maximal release coinciding with the phase of profound monocytopenia in the peripheral blood. Electron microscopy showed that circulating MPs could be directly visualized in the pelleted material obtained by ultracentrifugation of PPP, with diameters ranging between 0.1 to 0.5mum. Immuno-labeling of MPs demonstrated positive labeling with anti-TF antibody. Thus, LPS exposure in vivo causes both MP-associated and whole blood TF PCA to increase in a time-dependent fashion. The more prolonged increase in whole blood TF PCA probably reflects the presence of cell-associated TF which has a longer in vivo half life than MP-borne TF.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:713567 CAPLUS
DOCUMENT NUMBER: 135:271900
TITLE: Anti-tissue factor antibodies with enhanced anticoagulant potency
INVENTOR(S): Kirchhofer, Daniel K.; Lowe, David G.; Presta, Leonard G.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2402596	A1	20010927	CA 2001-2402596		20010308
EP 1263960	A2	20021211	EP 2001-924131		20010308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003527861	T	20030924	JP 2001-569367		20010308
AU 2001250814	B2	20070215	AU 2001-250814		20010308
PRIORITY APPLN. INFO.:			US 2000-189775P	P	20000316
			WO 2001-US7501	W	20010308

AB The invention concerns anti-tissue factor (anti-TF) antibodies with enhanced anticoagulant potency, and methods and means for identifying, producing and using such antibodies. The anti-TF antibodies of the present invention are designed to comprise a region binding to an epitope in the C-terminal macromol. substrate binding region of TF. The macromol. substrate is factor X or factor IX; the antibodies are monoclonal antibodies, humanized antibodies or human antibodies; and the disease is deep venous thrombosis, arterial thrombosis, stroke, tumor metastasis, arteriosclerosis, restenosis following angioplasty, acute and chronic inflammation, septic shock, septicemia, hypotension, adult respiratory distress syndrome and disseminated intravascular coagulopathy.

L3 ANSWER 11 OF 11 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER:	95313005 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 7792734
TITLE:	Complete inhibition of endotoxin-induced coagulation activation in chimpanzees with a monoclonal Fab fragment against factor VII/VIIa.
AUTHOR:	Biemond B J; Levi M; ten Cate H; Soule H R; Morris L D; Foster D L; Bogowitz C A; van der Poll T; Buller H R; ten Cate J W
CORPORATE SOURCE:	Center for Hemostasis, Thrombosis, Atherosclerosis and Inflammation Research, University of Amsterdam, The Netherlands.
SOURCE:	Thrombosis and haemostasis, (1995 Feb) Vol. 73, No. 2, pp. 223-30. Journal code: 7608063. ISSN: 0340-6245.
PUB. COUNTRY:	GERMANY: Germany, Federal Republic of
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:	English
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AB Gram-negative sepsis is oftentimes complicated by activation of coagulation with disseminated intravascular coagulation and microthrombosis. This may contribute to the associated morbidity, multiple organ failure and death. Recent studies have established that the tissue factor-dependent pathway of blood coagulation has a significant participatory role in the initial endotoxin-induced activation of coagulation. Tissue factor (TF), expressed on the surface of activated monocytes and

endothelial cells forms cell surface complexes with free circulating factors VII and VIIa. The latter complex proteolytically activates factors X and IX. Recent in vivo experiments have shown that a rapidly neutralizing TF monoclonal antibody prevents and arrests the endotoxin-induced activation of coagulation and similar studies have shown to reduce mortality in baboons. In this study we describe the preparation of a factor VII/VIIa neutralizing monoclonal Fab fragment and characterize its effect on in vivo activation of coagulation during experimental endotoxemia in chimpanzees. Four chimpanzees received a bolus intravenous injection of 4 ng/kg endotoxin in combination with Fab fragments of a factor VII/VIIa neutralizing murine monoclonal antibody (12D10) at a dose of either 50 micrograms/kg (n = 2) or 100 micrograms/kg (n = 2). Four control animals received a bolus injection of endotoxin alone. Administration of the 12D10 Fab fragments, immediately preceding the endotoxin bolus injection, effectively blocked the endotoxin-induced activation of coagulation. Plasma levels of products of in vivo activation, namely F1 + 2, TAT complexes and FpA remained at baseline values. The administration of 12D10 resulted in a rapid decline in factor VII/VIIa antigen levels which remained below 5 ng/ml for 180-240 min, followed by a rapid return to baseline levels.(ABSTRACT TRUNCATED AT 250 WORDS)